Citation:

Janszky I, Mukamal KJ, Ljung R, Ahnve S, Ahlbom A, Hallqvist J. Chocolate consumption and mortality following a first acute myocardial infarction: the Stockholm Heart Epidemiology Program. *J Intern Med.* 2009 Sep;266(3):248-57.

PubMed ID: 19711504

Study Design:

Population-based Case-Control Study

Class:

C - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

The purpose of this study was to assess the long-term effects of chocolate consumption amongst patients with established coronary heart disease.

Inclusion Criteria:

Subjects were Swedish citizens living in Stockholm County, 45-70 years of age, free of previous clinically diagnosed AMI.

Criteria for AMI included (the diagnosis 'acute myocardial infarction' required two of the criteria to be met):

- Symptoms consistent with AMI
- Positive blood levels of the enzymes CK and LD
- Specified ECG-changes

Exclusion Criteria:

Patients with diabetes mellitus.

Description of Study Protocol:

Recruitment

The investigators followed individuals enrolled as nonfatal AMI cases in the Stockholm Heart Epidemiology Program (SHEEP), a population-based case–control study of incident AMI. Male cases were identified during a 2-year period (1992–93) and female cases during 3 years (1992–94). Cases were identified through a special organization at the 10 emergency hospitals in the region.

Design: Population-based case-control study

Blinding used (if applicable): not applicable

Intervention (if applicable): not applicable

Statistical Analysis

The researchers used Cox proportional hazard models to examine the association between chocolate consumption and cardiac and all-cause mortality, new nonfatal AMI and hospitalization for stroke and heart failure.The group of never consumers was the reference category in these models. The investigators tested the proportionality of hazards using log-log curves and formal tests of interaction with time or log-time. Primary confounding factors for evaluation of chocolate consumption we included were age (in 5 categories), gender, smoking (in 3 categories), obesity, physical inactivity, alcohol consumption filtered coffee consumption (in cups per day), educational attainment and sweet score.

Rothman's synergy index with 95% confidence intervals was used to evaluate interaction between chocolate consumption and clinical characteristics. To examine potential mediators, the researchers calculated adjusted mean levels of biomarkers according to chocolate consumption and then compared the change in regression coefficients associated with chocolate modelled as a continuous variable from multivariable proportional hazards models with and without inclusion of specific biomarkers. For tests of linear trend, they treated the median value of chocolate intake in grams within categories as a continuous variable.

Data Collection Summary:

Timing of Measurements

Questionnaires about chocolate consumption were handed out a few days after the AMI incident. A health examination measuring blood pressure, height and weight with a blood sampling was undertaken 3 months after the AMI onset.

Dependent Variables

- Blood lipids, coagulation factors and inflammatory markers
- Glucose, insulin, insulin-like growth factor binding protein-1 (IGFBP-1), insulin resistance
- Hypertension was defined as (i) being on antihypertensive drug therapy, for the reason of hypertension, when included in the study; (ii) a history of regular antihypertensive drug therapy during the last 5 years (or a part of that time); (iii) a systolic blood pressure $\geq$170 mm Hg or a diastolic blood pressure $\geq$95 mm Hg.

Independent Variables

- The questionnaire distributed a few days after AMI onset queried the number of usual (50 g) portions of chocolate that participants usually consumed per day,per week or per month during the last 12 months. The original consumption categories included: never, less than once per month, 1–3 times per month, once per week, twice per week, 3–4 times per week, 5–6 times per week, once per day, twice per day and 3 times or more per day.

Control variables

- Age
- Smoking.Subjects who had never smoked regularly (i.e. for at least 1 year) were considered as neversmokers. Subjects, who smoked when included into the study or had stopped smoking within the last 2 years, were classified as smokers. Subjects, who had stopped smoking for more than 2 years before inclusion, were classified as ex-smokers.

  Obesity. Patients with a measured BMI-value over 30 kg/m^2 were classified as being obese.

Physical inactivity.Patients who reported inactive leisure time, which included occasional walks, during the last 1–10 years were categorized as physically inactive.

Alcohol consumption

Filtered coffee consumption

Educational attainment. Educational attainment was classified as mandatory school only versus high school, college or university.

Consumption of sweets and desserts.Patients were queried about their usual intake of six types of sweets – biscuits, cookies, cakes, pastries, confectioneries and ice cream, using the same response options as for chocolate. Each variable was categorized into quartiles and a value of 1–4 was assigned to each. The score values were added up to form a singlesweet score variable ranging from 6–24.

Description of Actual Data Sample:

Initial N:1381

Attrition (final N): 1169

Age: 45 to 70 years

Ethnicity: Swedish

Other relevant demographics:

Anthropometrics:

Location: Stockholm County, Sweden

Summary of Results:

Key Findings

There was an inverse, dose–response relationship between chocolate consumption and cardiac mortality both in age and gender-adjusted models and after controlling for other potential confounders. In contrast, sweet score had no statistically significant relationship to cardiac or total mortality.

When compared with those never eating chocolate, the multivariable-adjusted hazard ratios were 0.73 (95% confidence interval: 0.41 - 1.31), 0.56 (95% confidence interval: 0.32 - 0.99), and 0.34 (95% confidence interval: 0.17 - 0.70) for those consuming chocolate less than once per month, up to once per week and twice or more per week, respectively.

Those consuming chocolate less than once per month had a more substantially lower risk for stroke after the first 4 years of follow-up (HR 0.48, 95% CI, 0.20–1.18) than during the first half of follow-up (HR 0.91, 95% CI 0.39–2.08).

Chocolate consumption was also associated with lower cardiac mortality for patients with a BMI value below 30 kg/m^2 (HR for the trend variable 0.92; 95% CI 0.82-0.98), but not for those above this BMI (HR 1.01; 95% CI 0.91–1.11).

Author Conclusion:

Chocolate consumption was associated with lower cardiac mortality in a dose-dependent manner in patients free of diabetes surviving their first AMI. Although our findings support increasing evidence that chocolate is a rich source of beneficial bioactive compounds, confirmation of this strong inverse relationship from other observational studies or large scale, long-term, controlled randomized trials is needed.

Reviewer Comments:

Authors note the following limitations:

- *Chocolate intake might be associated with healthier lifestyle characteristics that could themselves explain the observed inverse association with cardiac mortality.*
- *It is also possible that some patients ceased chocolate consumption prior to hospitalization because of poor health*
- *Patients were not queried regarding dark and milk chocolate*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	N/A
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	N/A

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes

2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	Yes
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes

5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	Yes
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	N/A
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	???
7.1.	Were primary and secondary endpoints described and relevant to the question?	N/A
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	N/A
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	???
7.5.	Was the measurement of effect at an appropriate level of precision?	???
7.6.	Were other factors accounted for (measured) that could affect outcomes?	???

	7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**		Yes
	8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
	8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
	8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
	8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
	8.6.	Was clinical significance as well as statistical significance reported?	Yes
	8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**		Yes
	9.1.	Is there a discussion of findings?	Yes
	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes